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Angiographic Occurrence and Clinical Correlates of Intraluminal Coronary Artery Thrombus: Role of Unstable Angina

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The importance of intraluminal coronary artery thrombus in acute myocardial infarction is now recognized. Coronary thrombi, however, may be important in ischemic syndromes other than infarction. The coronary angiograms of 268 consecutive patients undergoing diagnostic angiography were prospectively examined for intracoronary thrombus and form the basis of this study. Of these patients, 29 (11%) (25 men and 4 women) met the criteria for coronary artery thrombus. Of the 29 patients with thrombus, 24 (83%) had unstable angina before angiography. The five remaining patients with thrombus had had a transmural myocardial infarction 3 to 18 months before cardiac catheterization. In 21 patients, the thrombus was distal to a significant stenosis; in 8 it was proximal to or at the site of a significant stenosis. Coronary artery thrombus was identified in 24 (35%) of 67 patients with unstable angina compared with only 5 (2.5%) of 201 patients with stable angina ($p < 0.0001$).

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The importance of intraluminal coronary artery thrombus in acute myocardial infarction is now well recognized (1–4), and thrombolytic therapy with streptokinase is gaining increasing acceptance in the management of acute infarction (5,6). Coronary artery thrombus may be important in other clinical subsets (7); however, there are no prospective data regarding its frequency in patients with other clinical manifestations of coronary artery disease (such as stable or unstable angina) who require diagnostic coronary angiography. Two retrospective studies of small numbers of patients have suggested an increased occurrence of coronary artery thrombus in patients with unstable angina (8,9).

The purposes of this study were: 1) to prospectively determine the angiographic occurrence of coronary artery thrombus in patients referred for angiographic evaluation of coronary artery disease, and 2) to define the clinical profile of patients with angiographically demonstrated coronary artery thrombus.

Methods

Patient selection. The coronary angiograms of 300 consecutive referred patients who underwent elective diagnostic angiography from August 12, 1982 to October 20, 1982 were prospectively reviewed for the presence of coronary artery thrombus. Of the 300 patients, 32 who were referred because of valvular heart disease were subsequently excluded from further analysis. No patients who were receiving thrombolytic therapy for acute infarction were included in the study. Thus, 268 patients formed the basis of this study.

Angiographic procedure. All angiograms were obtained with either the Sones or the Judkins technique with patients in the postabsorptive state after the intravenous administration of diazepam. Heparin, 2,500 units, was administered to each patient after peripheral arterial entry. Selective coronary injections were performed in multiple views using a contrast medium (Renografin-76) and recorded on 35 mm cine film. All angiograms were reviewed for the presence of thrombus independently by two experienced angiographers without knowledge of the clinical situation. Agreement of both angiographers was necessary for a thrombus to be declared present. In cases of disagreement, a third angiographer's opinion was decisive; only three such instances occurred.

Definitions. *Criteria for intracoronary thrombus.* Intraluminal coronary artery filling defects thought to be consistent with thrombus were defined as 1) contrast medium staining at the site of an abrupt occlusion of a vessel (Fig. 1), or 2) the presence of a filling defect surrounded by contrast medium seen in multiple views in the absence

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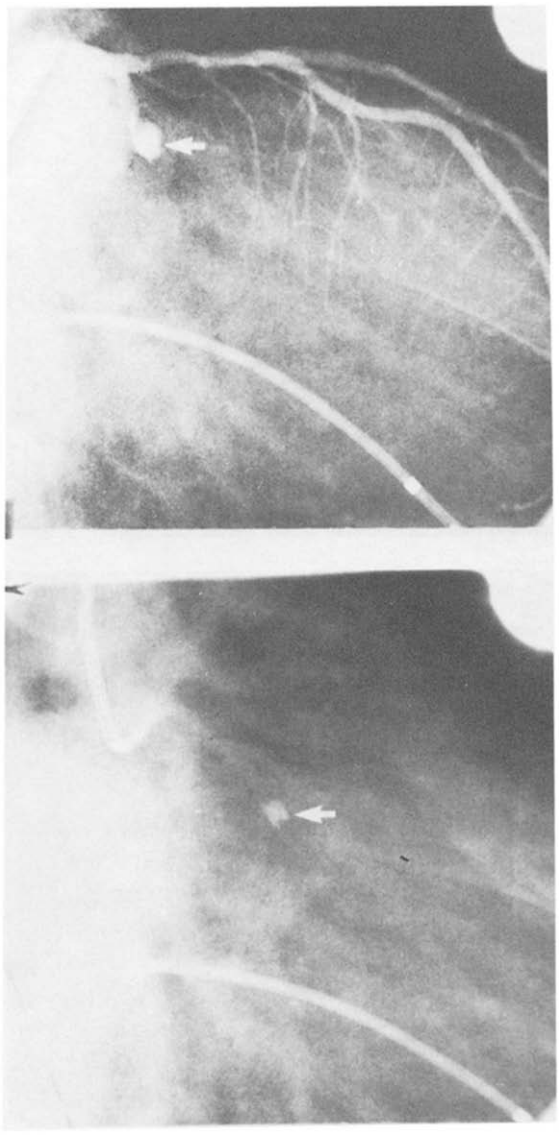


Figure 1. Angiograms of circumflex coronary artery. **A**, Right anterior oblique view, showing abrupt occlusion (**arrow**). **B**, Later frame of **A**, demonstrating contrast medium staining in area of abrupt occlusion (**arrow**).

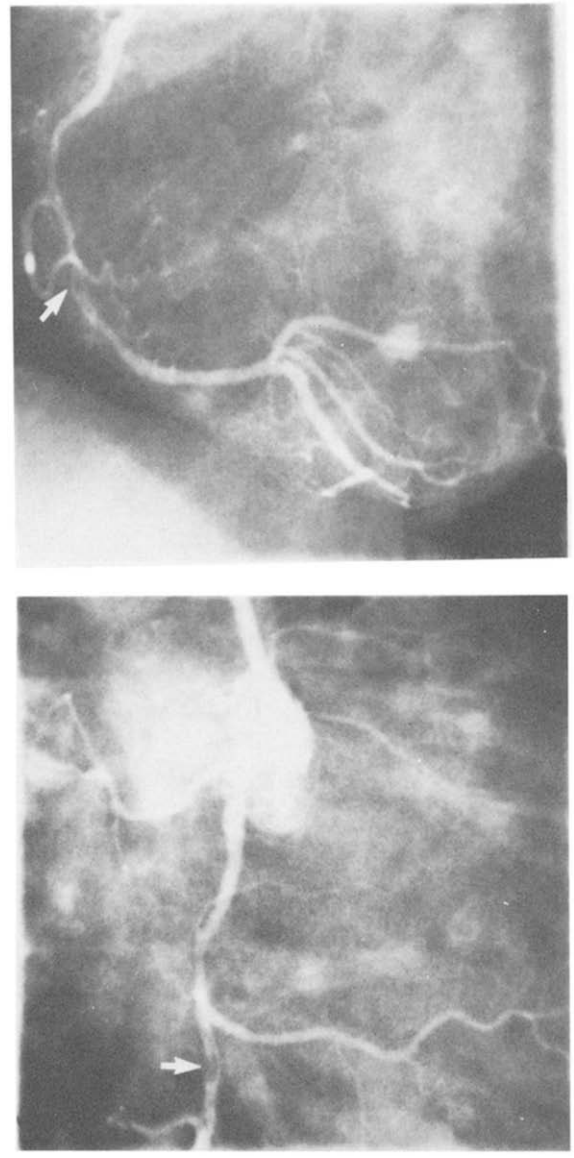
of calcium in the defect (Fig. 2). A thrombus was thought to be present if it fulfilled one of the two criteria and was identified independently by two angiographers.

Unstable angina. Unstable angina was defined as angina at rest or a substantially new pattern of chest pain that had begun during the preceding 2 months. In addition, pain at rest or continued pain during the postinfarction period in patients with a previous subendocardial infarction was also defined as unstable angina.

Results

Occurrence. Of the 268 patients, 29 (11%) had angiographic evidence of coronary artery thrombus. Of these 29 patients, 21 (72%) had a thrombus distal to a significant stenosis (70 to 99% reduction in arterial diameter) and 7 (24%) had a thrombus proximal to a significant obstruction (80 to 100% reduction in arterial diameter). One patient had contrast medium staining of a thrombus at the site of a 100% occlusion. Another had thrombus proximal to both a total occlusion in the right coronary artery and a 95% stenosis of the circumflex artery. Electrocardiographically, he had Q waves in leads II, III and aVF from a previous inferior myocardial infarction incurred 6 years earlier. He presented with acute ST-T wave changes in leads V_5 and V_6. In all patients, the location of the thrombus corresponded with electrocardiographic changes in those leads corresponding

Figure 2. Angiograms of right coronary artery. **A**, Left anterior oblique view, showing thrombus (**arrow**) distal to a high grade stenosis. **B**, Right anterior oblique view, demonstrating thrombus (**arrow**).



to the areas of myocardium served by the artery that contained the thrombus.

Of the 29 patients with thrombus, 24 (83%) had unstable angina pectoris and 13 of these had continued unstable angina after a recent nontransmural myocardial infarction. All five of the patients who had intracoronary thrombus without unstable angina pectoris had had a transmural myocardial infarction 3 to 18 months before cardiac catheterization. The one patient with unstable angina and thrombi in two vessels previously mentioned had had an inferior myocardial infarction 6 years before his acute presentation.

Location of thrombus. Of the eight patients with thrombus proximal to or at the site of a significant stenosis, seven had unstable angina, two of whom had had a nontransmural myocardial infarction within the 8 weeks before catheterization. The remaining patient without unstable angina had had a myocardial infarction 9 months before catheterization.

Of the 21 patients with thrombus distal to a significant lesion, 17 had unstable angina. The four remaining patients had had a transmural myocardial infarction 3 to 18 months before cardiac catheterization. There was no correlation between the site of thrombus relative to the stenosis and the clinical presentation (Table 1).

Prevalence of unstable angina. Of the 268 patients studied, 67 (25%) presented with unstable angina pectoris. Intraarterial coronary thrombus, either proximal or distal to a significant stenosis, was present in 24 (36%) of these 67 patients. The characteristics of patients with unstable angina pectoris with or without thrombus are described in Table 2. Three patients with unstable angina received full heparin therapy before cardiac catheterization: two because of continued angina while receiving maximal medical therapy and one because of recurrent cerebral transient ischemic attacks. One of the patients who receive heparin and continued to experience severe angina had angiographic evidence of intracoronary thrombus, but the other two patients did not. The differences between the patients with or without thrombus with regard to mean age, sex distribution, severity of coronary artery disease, percent receiving antiplatelet agents or heparin were not significant. More patients with unstable angina without, than with, thrombus at angiography presented with a sudden increase in the frequency of pain, new onset of pain or pain at rest. Because of the small number of patients, this difference did not reach statistical significance ($p = 0.06$). Patients with thrombus had more frequently had a subendocardial myocardial infarction with continued pain in the postinfarction period ($p < 0.02$).

In contrast, of the 201 patients without unstable angina, only 5 (2.5%) had angiographic evidence of intracoronary artery thrombus. The difference between the occurrence rate of coronary artery thrombus in patients with unstable angina (36%) and that in patients without unstable angina (2.5%) was significant ($p < 0.0001$).

Table 1. Clinical Presentation of 29 Patients in Relation to Site of Coronary Artery Thrombus Relative to a Stenosis*

Clinical Feature	Site of Thrombus	
	Proximal	Distal
Patients (no.)	8	21
Men	8	17
Women	0	4
Mean age (yr)	54.6	58.5
Diseased coronary vessels (mean no.)	2.37	1.86
Unstable angina (no.)	7	17
Previous infarction (no.)	1	4

*Differences between patients with thrombus proximal to a stenosis and those with thrombus distal to a stenosis were not significant.

Table 2. Comparison of Clinical Features of 67 Patients With Unstable Angina With or Without Thrombus

Clinical Feature	Thrombus	
	Yes	No
Patients (no.)	24	43
Men	19	35
Women	5	8
Mean age (yr)	58.3	60.0
Diseased vessels (mean no.)	2.0	2.26
Receiving antiplatelet agents (no.)	7	7
Receiving heparin (no.)	1	2
New onset of pain (no.)	16	21*
Rest pain (no.)	10	15
Sudden increase in frequency of pain (no.)	3	14
Pain with unstable angina after subendocardial infarction (no.)	13	11†

*$p = 0.06$; †$p < 0.02$.

Discussion

Angiographic diagnosis of coronary thrombus. Previous studies have identified angiographic criteria for acute coronary thrombus that include a central filling defect or staining at the site of an abrupt occlusion. The criteria have been validated in surgical and pathologic specimens (1,8). The sensitivity and specificity of angiography for the identification of thrombus remain unknown. In a series of patients who had acute myocardial infarction without angiographic evidence of coronary artery thrombus, thrombi were found at operation in 5 (25%) of 20 patients. Patients with acute infarction are known to have a high occurrence of coronary artery thrombus (1). Small thrombi or those adherent to the vessel wall may be hard to detect angiographically; thus, angiography may actually underestimate the true frequency of coronary artery thrombus. It could be argued that thrombus responsible for the clinical syndrome may undergo organization and, thus, be difficult to distinguish from atherosclerotic plaque. The time required for

such organization to occur is uncertain, and the abrupt onset of unstable angina leads us to suspect that the thrombus may be responsible for the sudden chanage in clinical condition. Although angiography may fail to detect small coronary artery thrombi, in some patients the angiographic appearance of an intraluminal filling defect may not represent thrombus. This is a potential problem in patients who have recanalized occluded coronary arteries and multiple intraluminal channels. Recently, asymmetric eccentric lesions were found by Ambrose et al. (10) to be present more frequently in patients with unstable angina. They postulated that the appearance of these lesions represented rupture atherosclerotic plaques or partially occlusive thrombi, or both.

The location of a thrombus distal to a significant stenosis may be the result of either stasis or turbulence of blood in the areas of slow flow beyond the stenosis. The presence of a thrombus proximal to a stenosis is more difficult to explain. It could be due to transient complete occlusion of a vessel, such as might occur with spasm, with thrombus formation and proximal propagation of the thrombus. It is also possible that in these patients the stenosis was actually due to thrombus propagation.

Clinical importance of coronary thrombus. The importance of thrombi in the coronary circulation has been documented in experimental models. In dogs with partially obstructed coronary arteries, Folts et al. (11) demonstrated a cyclic reduction in coronary flow due to platelet aggregates. This mechanism may also be active in human subjects. Rao et al. (12) showed an enhanced contribution of platelets to the intrinsic coagulation system in patients with coronary artery disease.

In the consecutive patient group of this study, coronary artery thrombus was found in 11%. In those patients with thrombus, 83% had unstable angina pectoris. Of all the patients with unstable angina, only 36% had coronary artery thrombus demonstrated angiographically. Thus, the difference in the presentation of patients with unstable angina with and without thrombus at angiography may be due merely to the relative lack of sensitivity of angiography in detecting the presence of very small or microthrombi.

Therapeutic implications. That coronary thrombi play an important role in unstable angina has important therapeutic implications. Lewis et al. (13) studied the effect of aspirin on the incidence of infarction or death in patients with unstable angina. In 1,266 men with unstable angina, the incidence of death or acute myocardial infarction was 51% lower in the group receiving aspirin than in the placebo group. Lawrence et al. (14) performed a prospective controlled study of intravenous fibrinolytic therapy in a small group of patients. One group with unstable angina was treated with intravenous streptokinase followed by warfarin therapy. The control group was treated with warfarin alone. There was a significant reduction in cardiovascular events in the streptokinase-treated group compared with control subjects. Mandelkorn et al. (7) demonstrated clinical and angiographic improvement in 11 of 19 patients given thrombolytic therapy who presented with unstable angina or nontransmural infarction. Vetrovec et al. (15) demonstrated a high rate of intracoronary thrombi in 12 patients with preinfarction angina and observed a decrease in frequency of angina after thrombolytic therapy. However, in the study by Rentrop et al. (6), five patients with unstable angina had no angiographically demonstrable change in luminal diameter at the site of subtotal occlusion after streptokinase therapy. Clinical improvement was attributed to reductions in preload and afterload. In this setting, fibrinolytic therapy may have been beneficial in lysing thrombi too small to be detected angiographically. Thus, antiplatelet agents, anticoagulation and thrombolytic therapy may have increasing roles in the management of patients with unstable angina.

It is now the practice at our institution to administer heparin to patients with unstable angina in whom there are no contraindications and whose condition cannot be easily stabilized with conventional medical therapy before angiography. In addition to thrombolysis, percutaneous transluminal coronary angioplasty has been performed safely and effectively in patients with unstable angina (16–18). The angiographic presence of thrombus at the time of balloon angioplasty, however, may adversely affect results. Mabin et al. (19) showed that the presence of coronary artery thrombus at the time of coronary angioplasty is a marker for an increased incidence of abrupt occlusion during this procedure. Perhaps sequential use of intracoronary streptokinase for thrombolysis followed by balloon angioplasty, as has been done successfully in evolving myocardial infarction, would reduce the incidence of abrupt occlusion (20–24).

Conclusion. The finding of coronary artery thrombus with angiography is not infrequent, occurring in 11% of patients in this series. Coronary artery thrombus was found most frequently in patients with unstable angina pectoris. Of the patients with intraluminal coronary artery thrombus according to angiographic criteria, 83% had unstable angina. Conversely, 36% of patients with unstable angina had coronary artery thrombus. Coronary artery thrombus was not found in patients who had stable angina without a prior myocardial infarction.

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